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THE MILROY LECTURES ON KALA-AZAR

II. Kala-azar as a Disease

Leonard ROGERS

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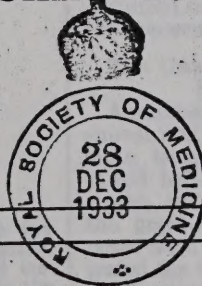
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ASSISTED BY

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the *BRITISH MEDICAL JOURNAL* of December 23rd, 1876, was operated upon in the Manchester Royal Infirmary in 1874, and since that date—as far as I have been able to ascertain—only 2 cases of cystine calculi have been met with in the hospital, one under the care of Mr. Walter Whitehead about twenty years ago, and the other under the late Professor Jones in 1892.

An interesting point in connexion with the latter case, as illustrating the hereditary character of cystine, is the fact that the patient, an unmarried female, aged 20 years, was the daughter of one of the four patients (also a female) operated upon by my father 24 years previously. She was admitted suffering from renal symptoms, and nephro-lithotomy was performed by Professor Jones, a small cystine calculus being successfully removed from the left kidney.

I have recently had an opportunity of examining a specimen of the urine of this patient, and find that at the present time (14 years after the operation) it still contains crystals of cystine in small quantity.

It is interesting to note, as illustrating the persistence of cystinuria, that an examination of the urine of her mother, eight years after the operation for the removal of the calculus from her bladder, also showed that cystine was still present. This patient had no further urinary trouble, and recently died of paralysis (34 years after the operation), at the age of 67.

The following are the details of the two cases recently under my care:

CASE I.

Cystine Calculus Removed by Suprapubic Lithotomy.

W. S., aged 32, was admitted October 17th, 1906, with the following history: Seven years previously he was suddenly seized with severe pain in the left lumbar region, and shortly afterwards he passed, per urethram, a small calculus, which was not preserved. Fifteen months ago he suffered from a

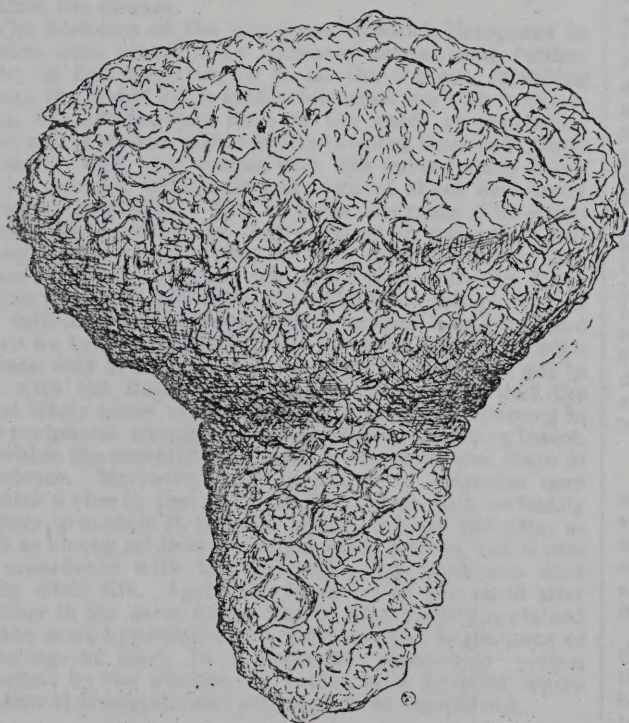


Fig. 1.— $\times 2$ lin.

similar attack of renal colic. He was then free from any symptoms until about two months previous to admission, when he began to be troubled with pain and increased frequency in micturition, and occasional sudden stoppage in the flow of urine. Blood had never been noticed in the urine, which was clear and acid, containing a trace of albumen. On sounding the bladder a calculus of large size was readily felt. Suprapubic lithotomy was successfully performed, and the patient made a good recovery from the operation. The calculus, which is mushroom-shaped, measuring $1\frac{1}{2}$ in. by $1\frac{1}{2}$ in., consists of cystine, and is of a pale yellow colour, with an irregular crystalline surface (Fig. 1). Examination of the urine subsequent to the operation showed that crystals of cystine were present on some days, while on other days none could be detected. No history of calculi in any other member of his family could be obtained.

CASE II.

Cystine Calculus Passed per Urethram.

C. W., 22, single, was admitted October 19th, 1906, with the following history: For about six months she had suffered from frequent attacks of pain, which commenced in the region of the left kidney, and extended across the abdomen and downwards into the thigh. About a month before admission, after a more severe attack than usual, followed by blood in the urine and increased frequency in micturition, she passed a small calculus. After this the attacks of pain became less frequent and less severe, and when admitted into hospital they had almost ceased, though the region of the left kidney was slightly tender upon pressure, and more resistant than on the opposite side. A radiograph gave a negative result. The urine, 1020, acid, was of a pale amber colour, and, examined microscopically, was found to contain the characteristic crystals of cystine, mixed with a few crystals of oxalate of lime. On some days the cystine crystals were present in such quantities that they could be seen with the naked eye, forming a deposit upon the cloud of mucus, which settled on standing, and glistening brightly if the specimen glass was held and rotated in the sunshine or electric light.

The calculus passed by the patient was pear-shaped, and of a pale yellow colour, with a glistening crystalline surface; it measured one-third of an inch in length (Fig. 2). The patient remained in hospital for three weeks, and as she was free from any attacks of renal colic she was then discharged, with instructions to return and report herself if there was any recurrence of the symptoms. On inquiring into her family history she was not aware that any of her relatives had ever suffered from symptoms of calculus.

I am indebted to my late house-surgeon, Mr. J. Stirling Young, for the accompanying drawings.



Fig. 2.— $\times 2$ lin.

The Milroy Lectures

ON

KALA-AZAR,

DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS
OF LONDON.

By LEONARD ROGERS, M.D., F.R.C.P., I.M.S.,
PROFESSOR OF PATHOLOGY, CALCUTTA.

LECTURE II.

KALA-AZAR AS A DISEASE.

[ABSTRACT.]

In my first lecture I dealt with kala-azar as an epidemic, tracing its origin, spread, and decline, and referred to a similar earlier outbreak in Bengal known as Burdwan fever. To-day I pass on to describe the disease itself—its course, complications, and terminations—and shall show you that it is not one whit less terrible when considered individually than collectively, for it literally kills by inches after most prolonged sufferings, which we are still powerless to check to any great extent. As the later stages of the disease are much better known than the earlier ones, it will be clearer if I first describe the typical advanced condition, returning to the still rarely recognized commencement of the fever.

THE GENERAL APPEARANCES IN THE CHARACTERISTIC STAGES OF THE DISEASE KALA-AZAR.

A number of lantern slides showing groups of cases were shown, and the salient points of each pointed out, the main features being the marked contrast between the tumid bellies due to the very great enlargement of the spleen, and sometimes also of the liver, contrasting with the great wasting of the chest, face, and limbs. Brief notes were given of a group of hospital cases which illustrated the different courses the disease might take, while a village group showed the great frequency of the affection in children, just as in malarial fever, the incidence decreasing steadily in the subsequent decades. Other groups of sporadic cases, then known as "malarial cachexia" in the Sylhet Valley, which was not invaded by the epidemic, showed the clinical identity of the two forms of the disease, which was the principal argument of the speaker in his 1897 report in favour of his view that the epidemic disease in the Brahmaputra Valley was but an intensified form of malarial fever. The extreme wasting in the last stages and the dropsical ascitic form

produced by a peculiar form of intracellular cirrhosis of the liver were also illustrated.

FAMILY DISTRIBUTION.

Several of the cases already referred to illustrate very well the extraordinary tendency of this disease to attack a number of persons in the same family or household, but the frequency with which this is the case will be better realized from the following figures relating to twenty successive Assamese patients seen in the Nowgong Hospital. Among their near relatives no less than 123 persons had been attacked by kala-azar, only 2 of whom recovered from it, while but 44 of their near relatives had escaped the infection; or to put it another way, no less than four-fifths of these patients had lost half or more than half of their relatives within three to five years, so that it is easy to understand how whole families have been destroyed, and so much land has fallen out of cultivation.

A similar family incidence is seen in the sporadic disease, and is best illustrated by European series of cases, in whom it is easier to follow up the histories. An examination of my notes of the Calcutta European Hospital cases of the last six years shows that the most common relationships between patients actually in hospital for the disease were parent and child in six instances, and brothers and sisters in seven more, nearly always children, while in no less than three of these instances more than two children of the same household were admitted, the series in one family extending over a period of five years. Moreover, just one-third of the whole series of cases had relations actually in hospital during this period, while a good many more gave histories of other members of their families being attacked with fevers of long duration, which were pretty certainly mostly of the same nature. This family incidence clearly points to a house infection, and was the basis of the successful measures I advocated against the disease.

The histories of the rare cases in which Europeans in Assam were attacked by kala-azar throw some further light on this question, for in all the 6 cases, regarding whom Dr. Dodds Price kindly furnished me with information, the affected men were in the habit of cohabiting with native women either in the infected lines or in three instances with one woman, who was subsequently found to be infected with kala-azar, two of them eventually dying of the disease. Two of these last cases of infection were most important, as they occurred in parts then uninfected with kala-azar, but in each case the woman had come from an infected district. Moreover, Dr. Price knows of no instance in which a European cohabited with an infected native woman who escaped kala-azar; and when we bear in mind that it is the usual custom for such women only to come to the bungalow at night and not to eat with the European, then it becomes clear that the most likely mode of infection by a parasite occurring in the peripheral circulation is through some biting insect, in which the parasite may pass its extracorporeal stage of existence. Moreover, such a source of infection may furnish a clue to that of adult Europeans, with no family history to explain it, in large towns such as Calcutta, as well as among soldiers in Bengal cantonments, and is also in accordance with the decreasing age incidence after early adult life. Again, the infection of one child after another in the same house may be also readily explained on the same hypothesis, and indicates the importance of isolating—at least, in a separate room—any person attacked by the disease, or, better, in a hospital where persistent treatment and nursing can be carried out.

AGE AND SEX INCIDENCE.

Among tea-garden coolies, who furnish the most accurate statistics, there was no difference in the incidence of the disease on the two sexes, nor did occupation affect it. Numberless instances of husband and wife being infected one after the other were met with, it being, in fact, the exception for one of them to escape—another striking instance of house infection. In the sporadic disease in Calcutta an excess of native males are admitted, much in proportion to those of other diseases. In the European hospital there were twice as many males as females above the age of 15, possibly partly due to the source of infection just mentioned; but in children under 15 there were 23 females to 13 males, probably due to a larger proportion of the male children living away from home at schools.

The age incidence is of great importance, the most striking fact being the number of children attacked. In my report I recorded that 25.6 per cent. of my cases occurred in children under 10, while 24.4 per cent. more were between 10 and 20 years old, making 50 per cent. under the latter age. Further, in a more recent report on the sporadic disease in Sylhet, 39 per cent. were under 10, and 30 per cent. more between 10 and 20, making nearly 70 per cent. under 20. Among natives in Calcutta only 8 per cent. were in children under 10, but 40 per cent. between 10 and 20, three-fifths of which were boys from 10 to 15, who are much more readily brought to hospital than girls or younger children. Between the ages of 20 and 30 were 32 per cent., 16 per cent. from 30 to 40, and only 4 per cent. over 40 years of age. Among Europeans, who readily bring their children to hospital, 20 per cent. were under 10, and 22 per cent. more between 10 and 15, making no less than 42 per cent. 15 or under; 22 per cent. from 20 to 30, and 20 per cent. over 30, showing once more a very high rate among the unfortunate children, and a decreasing one with advancing years.

RACE INCIDENCE.

It has already been mentioned that epidemic kala-azar was rare in Europeans in Assam compared with natives, but is not so very uncommon in Europeans in Calcutta in the sporadic form. The class of Europeans attacked is here of great importance, for out of 87 cases, regarding whom I have a note as to how long they had been in India, I find that no less than 87.34 per cent. were born and bred in that country, and only 12.66 were immigrants from Europe. Moreover, the shortest time after arriving in India that any immigrant was attacked was eight years; a second had been thirteen years, and a third nineteen years in the country; while the remaining eight had all been over twenty years in India, and belonged to the same class as those born in Calcutta, and, like them, were living in parts of the city where their houses were surrounded by those of native inhabitants and under conditions of overcrowding and bad sanitation. In fact, almost all these unfortunate people belonged to the poorest sections of the mixed European and native population, among whom the sanitation and cleanliness of the well-to-do official and commercial European immigrant class is an impossibility—a fact of great importance in connexion with the etiology of the disease. In marked contrast with this is an observation I have recently made to the effect that 80 per cent. of the European immigrants admitted to hospital for typhoid in Calcutta had been three years or less in India, for the totally different incidence of sporadic kala-azar just mentioned in this class will prove a useful point in the differentiation of the later disease in its early remittent stage from typhoid, with which it has been so much confused.

SEASONAL INCIDENCE.

Owing to the disease lasting from a few months to several years, cases are admitted to hospital at all seasons, and neither in Calcutta or Madras is there any very marked seasonal incidence, although there is some excess of admissions of Europeans in Calcutta at the end of the cold and beginning of the hot season, especially among those coming in the early stages of the fever.

Of much greater importance is the question whether the fever begins at any special season, as is suggested by the fact that the extra-corporeal stage of the parasite, to be described later, only developed in my cultures below a temperature of 75° F. It is very difficult to obtain accurate histories of the beginning of the disease in many cases, especially when they are seen for the first time at a much later date, but an analysis of my notes of those who stated they had had fever for not more than six months in two series of cases (in the Native Medical College and European hospitals respectively), both showed a marked preponderance commencing during the cold weather, or early in the hot weather, on account of the frequent long incubation period. These results can be summed up by saying that in the six months from November to April there were three times as many cases in the European series and almost four times as many in the native one as in the remaining six months of the year—a sufficiently striking fact when the difficulties of getting accurate data are considered. When in Assam I tried to work out this point from the admission to hospital for fever on tea

estates, and found that most of the patients suffering from typical kala-azar in the cold season had been admitted for short attacks of apparently malarial fever in the previous rainy season from June to October, but few escape malaria at that time. On finding the sporadic cases in Calcutta mostly began in the cold season in Calcutta, I wrote to Dr. Dodds Price for his matured experience on the subject, and he very kindly sent me histories of all his European cases, every one of which had commenced in the cold weather; while an inquiry into his, then comparatively few, native patients also showed that almost all of them had developed kala-azar during the cold weather, and he added, "All this is very instructive, and fits in exactly with your Calcutta experience."

Taking everything into consideration, I think there is sufficient evidence to prove that the great majority of patients become infected in the cold season, and I am inclined to think that infection will ultimately be found to be limited to this time of the year. The importance of this fact in connexion with prophylactic measures is clear, as it will greatly simplify matters if precautions against infection have only to be taken during a few months of the year.

THE TYPES OF FEVER.

I now come to the difficult subject of the diagnostic value of the types of fever in kala-azar, my conclusions being based on four-hour temperature charts of every case in the European Calcutta hospital for several years, and a still larger series in native patients; while as I also possess complete notes and charts of every fever case in the open wards of the European hospital for two years I am now in a position to point out the most important features in the diagnosis of kala-azar in the difficult early stages from other fevers with which they are commonly confused. The lantern slides prepared from the charts, some of which represent the temperature curves for several months, will best serve to illustrate the types met with.

The principal points illustrated by the charts shown were the following: The very long duration of the fever, which shows alternating remittent and intermittent types for many months at a time, even in the case of patients admittedly in a markedly cachectic and anaemic condition, showing the great resisting powers of the patients. When the temperature is of the remittent type there is rapid wasting and impoverishment of the blood, but when it falls to the low intermittent type, both the weight and the blood show steady improvement, while quinine in large doses has a marked effect in reducing the high dangerous type of fever to the low, comparatively harmless one, which may eventually wear itself out and cease entirely, when the weight is soon regained; and once the patient has been free from fever for several months, and fully regained the normal weight, relapses are rare and recovery is permanent and complete. Such cessation of the fever and cure sometimes follows a severe septic complication, such as cancrum oris, and is then accompanied by a marked rise in the previously very low number of polynuclear leucocytes, which the writer has also been able to produce, with good results in a few cases, by injections of sterilized cultures of staphylococci in accordance with the methods of Sir Almroth Wright, although it has not been invariably successful. The good effect of large doses of quinine was illustrated by a nine months chart of a child of 8, seen early in the disease, and whose fever was only finally broken when 50 gr. of quinine had been taken daily for seven weeks; her weight also steadily rising from the time this large dose was given, and no ill-effect being produced by it.

The recognition of this fever in its early stage, which usually begins with a high remittent form of pyrexia, may often be accomplished by noting the certain peculiarities in four-hour temperature charts. The most important of these, which is illustrated by the slides shown, is what I have already described as the double remittent type, namely, a marked daily double or even a triple rise of the temperature, often for several days together, in the absence of any treatment by the more powerful sweat-producing antipyretic drugs such as antipyrin. This double type is most frequently seen in the earlier periods of the fever, but may occur at any time in its course, and may also occasionally appear during continued or intermittent pyrexia in kala-azar. The great importance of this type is that, in my

experience, it is never seen in typhoid fever, for which the early stage of sporadic kala-azar is so frequently mistaken, as in some of the cases illustrated, and this type is almost diagnostic of the new fever, the first case in a European in Bombay having been first suspected on account of the double remissions taking place. Another type of fever shown in the charts, which is rather characteristic of this fever, is a low continued type of pyrexia, the temperature falling below 101° F., but not varying more than two degrees in the twenty-four hours; a type which is much rarer in typhoid, in which the pulse is also usually slower than in kala-azar in proportion to the degree of the pyrexia. Moreover, even when the fever is high for long periods in kala-azar there is a characteristic absence of severe distress or typhoid symptoms, patients often saying they feel quite well, and do not think they have any fever, when the thermometer registers 103° F. or 104° F. Once more, when the remittent temperature falls it commonly assumes a low intermittent type, rising to about 100° F. every afternoon, instead of running a subnormal course, as after typhoid, a feature that will often allow of the more serious kala-azar being suspected at an early date before the cachectic stage has been reached. A consideration of these various types will nearly always allow of the sporadic affection being suspected at an early date, when persistent treatment is most likely to be of avail, while the blood changes will allow of the diagnosis being confirmed.

THE SPLEEN AND LIVER IN KALA-AZAR.

Time will not allow of my giving a full clinical account of this remarkable disease (although I hope to do so shortly in a work on Fevers in India, for which I have been collecting material for a number of years), but a few of the more salient points must be touched on.

The Spleen.—The great degree of enlargement of the spleen can best be indicated by the following data. In 70 typical advanced cases of the epidemic disease in Assam of which I have notes, the spleen was enlarged in all, while in 94.5 per cent. it reached to at least 3 in. below the costal margin, in 56.5 per cent. it extended to the navel or beyond, and in 27.7 per cent. to the level of the anterior superior spine of the ilium. In 95 consecutive sporadic cases in the Medical College, Calcutta, all verified by finding the parasite in the spleen blood, in 80 per cent. the organ reached to the navel or beyond, and in 10 per cent. to the anterior superior spine of the ilium. In a series of earlier sporadic cases at the European general hospital the spleen extended to the navel or beyond in 63 per cent., being nearly always of this size in cases of over three months' duration, although the edge was above the navel in three-fifths of the cases with under one month's history of fever.

On the other hand, among 200 healthy coolies I examined in Assam on a tea-garden when unaffected with kala-azar, I found only 1 per cent. with spleens reaching down to the navel, in only 6 per cent. did it extend 3 in. below the ribs, while in a total of 25 per cent. the organ could be felt below the ribs—figures which suffice to disprove Dr. Giles's statement that it would be absurd to attach any importance to enlargement of the spleen in kala-azar in such a malarious country as Assam.

The liver was enlarged in 43 per cent. of my Assam series, in 75 per cent. of the Medical College, and in 59 per cent. of the European cases in Calcutta who came earlier under observation, it having been normal in seven-eighths of the European patients admitted during the first month of the fever. The enlargement of the liver to any marked degree is very uncommon in the earlier stages, although after some months it may occasionally reach down to the navel, and may then be even larger than the spleen, and eventually become cirrhotic, causing ascites.

THE BLOOD CHANGES.

I have elsewhere described the blood changes in kala-azar, and pointed out their great value in differentiating it from other diseases, especially fevers, so need only now summarize them. In the first place, an increase in the percentage of the large mononuclear leucocytes is very common, and of great value as a point in the differentiation of the early stages of sporadic kala-azar from typhoid fever, for in the latter the lymphocytes, but very rarely the large mononuclears, are increased during the pyrexia. On the other hand, this change is of no help in dis-

tinguishing kala-azar from true chronic malaria, in which a large mononuclear increase is also commonly present. These two last diseases may, however, be distinguished by counting the total red and white corpuscles and working out the proportion between the two; for in malaria both are about equally reduced, so that the ratio of white to red remains normal, namely, about 1 to 750, and very rarely, if ever, falls below 1 to 1,000, while in kala-azar it is the rule for the white corpuscles to be disproportionately reduced, so that the ratio of white to red is—in the absence of any leucocyte-increasing complication—commonly below 1 to 1,500, and not rarely as low as 1 to 2,000, 3,000, or more. This extraordinary reduction of the leucocytes, which not rarely number but from 500 to 1,000 per c.cm., is almost diagnostic of kala-azar, as I have never met it in any other fever cases out of some hundreds in which I have done blood counts, and it has often enabled me to diagnose the disease in a comparatively early stage. So much is this the case that I now rarely employ the spleen puncture as a diagnostic measure, several fatal cases, in addition to those published, having come to my knowledge. It should never be done in very anaemic patients, or in those who have suffered from any form of haemorrhage, unless the blood is first proved to be clotting normally, while I always take the further precaution of keeping up digital pressure for several minutes after withdrawing the needle, and immediately administering a dose of calcium chloride by the mouth. With these precautions it may be of value in some difficult comparatively early cases in which the confirmation of the diagnosis is of great importance, in order to allow of continued and adequate treatment being strongly urged on the patient, so many of whom leave hospital during a temporary remission of their fever, and leave off the all-important quinine until a fresh high remittent bout comes to reduce them another step towards the grave.

COMPLICATIONS.

The frequency with which kala-azar is terminated by some inflammatory complication has already been mentioned and may best be illustrated by the data from 40 necropsies made by me at the Medical College Hospital. All but 7 of them showed some serious local disease, and some of them more than one. In 11 pneumonia, in 10 dysentery, in 7 cancerum oris, in 2 each pneumococcus meningitis, purpura, cerebral haemorrhage, and phthisis respectively, and in 1 pericarditis were found, while in several cancerum oris cases staphylococci or streptococci were cultivated from the spleen, revealing a general septic infection. The extreme reduction in the polynuclear leucocytes in this disease, in which they not rarely fall to one-twentieth or less of the normal numbers, easily explains the frequency with which these patients fall victims to the specific organisms of pneumonia, dysentery, phthisis, or the cocci of cancerum oris, in which I have never been able to find the diphtheria bacillus, which has been met with in European cases of this disease.

Haemorrhages deserve special mention among the complications, reduced coagulability having been found by me in some of these cases, while bleeding from sloughing ulcers, or from the stomach or bowel, has also been seen, in addition to several cases of bleeding into the brain or its membranes.

TREATMENT.

Although much has been done to elucidate the pathology of kala-azar during the last four years, unfortunately the treatment of the disease has made no corresponding progress, and is still in a most unsatisfactory state. In Madras, indeed, I am informed that almost every case is believed to die, the mortality being estimated at 98 per cent., the highest figure reached in the Nowgong tea estates by the epidemic form, while that of several hundred cases treated by Dr. Dodds Price at the height of the epidemic gave an average mortality of 96 per cent. Dr. Price's cases were treated with thymol first, to exclude ankylostomiasis, quinine in moderate doses being generally used during the several periods the patients were in hospital, but it was the common opinion that quinine failed to check the fever in the same way it did malaria, and many thought it quite useless and used it very little, as is also the case in Madras at the present time. In my report I strongly dissented from this view, and urged that quinine does have a definite effect in controlling the severity of fever, even when it did not stop it

altogether, and recommended that it should be given in large doses, and persisted with for months together if necessary. Several years' further experience in Calcutta has only served to confirm me in that opinion, for I have repeatedly seen a high remittent fever reduced to a comparatively harmless low intermittent one by increasing the quantity of quinine given, 60 gr., and in some cases 90 gr., a day having been taken for considerable periods with nothing but good effects beyond being sometimes distressing to the patients.

Once the temperature has fallen to the low intermittent type, it can often be kept down to that point for a long time by smaller doses, 20 gr. in the morning being commonly effectual. That this line of treatment gives far better results than those admitted by unbelievers in quinine will be clear from the fact that after the publication of my report, Dr. Dodds Price systematically tried persevering quinine treatment, and when he worked out for me the results of several years' experience, he found that the mortality of 500 consecutive cases was but 75 per cent., the remaining 25 per cent. having permanently recovered, against 4 per cent. in the earlier series quoted above. Now as these patients were indentured coolies, who remained working on the gardens, often for years, after getting over a typical attack of kala-azar (the diagnosis of which in its characteristic stages presents no difficulties to Dr. Price with his fifteen years' daily experience of the disease, while in some of them the parasite was also found by spleen puncture), there can be absolutely no doubt about their absolute recovery, some of them having also been seen by me both during and after their attacks.

Moreover, these unquestionable results of Dr. Price's are confirmed by my smaller experience in Calcutta under less favourable conditions for following up my patients. Thus, out of 65 cases in the European hospital during the last three years of which I have notes, 18 who left the hospital in a doubtful condition I have not been able to get further news of, leaving 47 other cases. Of these, 21 died either in hospital or after leaving it; 9 more, who left in a worse condition than they came, may be counted as having died—leaving 7, or 14.88 per cent., who left hospital after having lost their fever and greatly improved, a fair proportion of them probably recovering, and 10, or 21.27 per cent., have completely recovered and are known to have been well for from several months to upwards of a year after leaving hospital. It should be mentioned that three of the patients who recovered had also been treated with injections of staphylococcus vaccine, which appeared to have some good effect.

These figures are in close accordance with those of Dr. Price, and contrast most favourably with nearly invariably fatal results admitted by those who still deny their patients the benefit of persistent cinchonization, although without any efficient remedy of their own, and I venture to think that, in view of the above data, my line of treatment should never be neglected until we have a better one to replace it, as I hope and expect will be the case in time. Bone marrow tabloids, to repair the blood deterioration, are also of considerable value, while atoxyl, which is now being advocated in the allied protozoal disease, sleeping sickness, is worthy of trial, for my friend, Dr. J. Megaw, I.M.S., has injected it in two cases with at least temporary good effects. Colonel Lukis, I.M.S., Principal of the Medical College, Calcutta, has also tried cinamate of soda to increase the leucocytes, but without accomplishing the desired result or doing any good; and x rays over the spleen have been tried by the same observer, but without effecting any cures. In view of the chronicity of the disease, and the occasional remarkable spontaneous recoveries from an apparently hopeless state, much caution is required in making deductions regarding any line of treatment, but the extraordinary cures which do occur encourages the hope that a better treatment even than the quinine one will be found to rescue these unfortunates from the lingering death which still awaits the great majority of them.

THE DISTRIBUTION OF SPORADIC KALA-AZAR IN INDIA.

Since it became known that so many cases previously classed as "malarial cachexia" are but the sporadic form of kala-azar, observations on its distribution have been accumulating. Donovan and others have found it to be very common in Madras, while my own observations have

shown it to be widely distributed all over Lower Bengal and Assam, except the eastern part of the Brahmaputra Valley. It also occurs somewhat less frequently in Western Bengal or Bihar, and extends into the neighbouring eastern end of the United Provinces of Agra and Oudh, cases in soldiers having been verified by the officers of the Royal Army Medical Corps at Benares, while I have also seen two who appear to have contracted the disease in Allahabad, and others have been met with among Gurkhas as far west as Dehra Dun. On the other hand, during an examination of the records of all the fever cases admitted to the Lahore Medical College Hospital for three years I failed to find any cases resembling sporadic kala-azar, while it is also specially noteworthy that I met with no double remittent, low continued or other doubtful long fevers among them. The Bombay records also show a similar absence of the disease, except rare importations from Madras, so that the disease appears to be limited to the eastern side of India, although I am informed that Burmah, like Bombay, only has cases contracted at Madras.

In connexion with this distribution it is of interest to note that the areas affected all have a very mild cold season, during which the mean temperature for three or four months remains between 60° to 75° F., for I shall show in my concluding lecture that these are the limits between which I have been able to cultivate the parasite outside the human body. On the other hand, in the unaffected north-west parts of India the mean temperature during the cold months falls lower, while owing to the brevity of spring and autumn in India, the temperature conditions most favourable to the organism outside the human body last a very short time in those areas.

EFFECTS OF SEASONAL VARIATIONS ON THE PREVALENCE AND ORIGIN OF THE DISEASE.

I have already shown that the infection of kala-azar is probably limited to the cold season, so an exceptionally long "cold weather" might be expected to temporarily increase the occurrence of the disease. This is actually so, for two years ago such a cold season occurred, and during it and the following early hot weather months an unusually large number of sporadic kala-azar cases were admitted to both the native and European hospitals of Calcutta—many more than in the following year, with a normal cold season. Now this long "cold weather" followed an early cessation of the previous monsoon rains, for the withdrawal of the south-west monsoon is succeeded by a cold north breeze; and it will be remembered that in my first lecture I pointed out that the Assam epidemic arose as a consequence of four out of five successive years of deficient rainfall in the early Seventies, due to an early cessation of the monsoon current. I have not been able to get complete meteorological data for Rungpore in the Seventies, but those of Calcutta of that period do show that during several of the years of deficient rain the mean temperatures of the ensuing cold season were below the average.

Now, if a single cold year had such a marked influence in increasing the sporadic kala-azar in Calcutta, on account of the longer period which was favourable to the infection, it becomes easy to understand how an unusual succession of such seasons might have increased the number of cases, and so the foci of infection, year by year, until the fever became so widespread that the people began to leave their villages, and thus carried the infection into areas at the foot of the Garo Hills and in the Goalpara subdivision, which had hitherto been almost, or quite, free from it, and so started the spreading disease in Assam in a people who were extremely susceptible to it, owing to not having previously suffered from the sporadic form. Such an origin of the Assam epidemic kala-azar is most in accordance with the known facts, and also with the life-history of the parasite and mode of infection, which I shall deal with in my remaining lecture.

THE Sleeping Sickness Commission of the Royal Society has issued a further report (No. VIII) which contains a continuation of the report on the disease in Uganda, by Lieutenant Gray, R.A.M.C., and the late Lieutenant Tulloch, R.A.M.C., a report on the disease in Unyoro and the Nile Valley, and an account of experiments on the power of tsetse flies to convey *Trypanosoma gambiense* by Mr. P. H. Ross, M.R.C.S., L.R.C.P., and three papers by Professor Minchin and others.

MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL.

THE TREATMENT OF ECZEMA.

It is now admitted that eczema is not caused by a parasitic organism. The coccus, which appears in mulberry-shaped masses, and which was named *morococcus* by Unna, is now thought to be a staphylococcus of low virulence frequently found on the skin. Sabouraud has shown that the vesicle of eczema is at first sterile, which quite puts out of court the presence of any specific micro-organism. It follows, therefore, that anti-germinal applications are not called for, and indeed have often made a pure and simple eczema much worse by irritating it. Care must be taken to exclude seborrhoeic dermatitis, which is only benefited by certain antiseptic remedies.

No doubt various food toxins and the products of imperfect metabolism and malassimilation by circulating in the blood can produce erythemata as well as other conditions of the skin, and if they cannot often produce an eczema, they may aggravate it and possibly produce it in a predisposed subject. To counteract this tendency, diet the patient, and prescribe correctives, of which salicin is one of the best in these cases. Water taken between meals is also helpful. All that is required locally are quieting and protective applications. If for any reason sodium chloride is retained beyond the normal quantity, the excess entails the retention of an additional quantity of water to hold it in solution. The surplus salt and water under certain circulatory conditions passes out of the blood into the tissues, and in this way eczema may be kept up. So that it may be necessary to lessen or cut off the common salt the patient is accustomed to take with food. So many cases of eczema are produced by susceptible individuals handling poisonous plants, such as the *Primula obconica*, as well as many chemical and other substances, that one has to be constantly on the look-out for this cause.

Eczema depending chiefly on a neurotic tendency, and usually occurring in people who are broken down in general health, is difficult to manage, and is not much benefited by ordinary treatment, unless a change into the country is insisted on. If this is not practicable, perhaps cod-liver oil does as much good as any internal remedy. Inquiry as to the amount of sleep the patient gets is also important, as there is no better restorative for nervous conditions.

It is almost unnecessary to mention that cleanliness of the eczematous surface should be carried out with a weak alcohol, as diluted methylated spirits; or, if the eczema is very acute, with weak warm gruel instead of soap and water. As Lionel Beale used to say, few people know what a healing remedy spirit is to the skin.

Where much thickening has occurred, and especially if fissures have formed, eczema rimosum, nothing does so well as local dressings of some reducing agent, as salicylic acid in various strengths. In severe cases of eczema, and when an extensive surface is involved, the good effect of rest should be remembered, and the patient confined to bed.

Although alcohol is valuable externally, it disagrees if given internally in eczema by dilating the peripheral vessels. It is not too much to say that if an adult's eczema is receiving suitable treatment to which it does not favourably respond, the abuse of alcohol should be suspected. If the surface of an eczema does not show much redness, a weak preparation of spirit and tar painted on once or twice in the twenty-four hours, in addition to the ordinary application, at once relieves the itching and cures the eczema if the case selected is found to tolerate this interference.

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OBSTRUCTION OF THE OESOPHAGUS.

THE report by Dr. H. E. Davison¹ of a case of oesophageal obstruction due to the presence of a bolus of meat, which he relieved by a timely dose of apomorphine, reminds me of a somewhat similar case I had the opportunity of seeing in the summer of 1906.

BRILL was called to see a woman, aged 52, who had, it was reported, swallowed a hard pea, and was choking. On my

